Adaptive Behavior in Stressful Situations and Stroke Incidence in Hypertensive Men

Results From Prospective Cohort Study “Men Born in 1914” in Malmö, Sweden

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Background and Purpose—Although hypertension is a major risk factor for stroke, many hypertensive persons remain healthy. The aim of the present study was to analyze whether adaptation in a stressful situation was associated with the incidence of stroke in hypertensive men.

Methods—Two hundred thirty-eight hypertensive men were followed from baseline in 1982/1983 until first stroke, death, or December 31, 1996. Adaptation to stress was studied with the serial Color-Word Test. In the Regression dimension, 4 patterns of adaptation could be distinguished according to mastering of the test. Successful mastering of the test was shown in stabilized patterns, increasing difficulty in cumulative patterns, fluctuating difficulty in dissociative patterns, and fluctuating difficulty that increased during testing in cumulative-dissociative patterns. The patterns were compared regarding stroke incidence.

Results—Forty-three men experienced a stroke during follow-up. Stroke rates per 1000 person-years were 12.6 for men with stabilized patterns, 14.3 for men with cumulative patterns, 16.2 for men with dissociative patterns, and 31.2 for men with cumulative-dissociative patterns. Multivariate analysis, adjusted for relevant cerebrovascular risk factors, showed that the cumulative-dissociative pattern of the Regression dimension was associated with an increased risk of stroke during follow-up (relative risk 3.00, 95% CI 1.32 to 6.81).

Conclusions—The specific behavior pattern, characterized by the greatest difficulties in managing the test, was associated with incidence of stroke in hypertensive men. One interpretation is that hypertensive men who chronically fail to find successful strategies in stressful situations are vulnerable to the damaging effects of stress and thereby at an increased risk of a future stroke.

Key Words: hypertension n neuropsychological tests n stress, psychological n stroke

Stroke is associated with huge costs, both economically and in terms of human suffering. Hypertension has been acknowledged as the major risk factor for stroke. The associated risk can be assumed to be modified by interaction with several other factors, because not all hypertensive individuals experience a stroke. In the case of myocardial infarction, many research programs have been aimed at delineating the relationship between incidence, psychological stress, and personality. The effects of stress and personality factors on stroke incidence have attracted far less interest.

Studies have, however, reported associations between stress and stroke. Severe psychological stress or life-threatening events have been related to an increased risk of both nonhemorrhagic and hemorrhagic strokes. General difficulties in coping with stress, as well as specific features of the type A behavior personality,

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patterns can be distinguished according to mastering of the test. The objective of the present study was to analyze whether adaptive behavior can be related to the incidence of stroke in hypertensive men.

Subjects and Methods

Study Population
The cohort study “Men Born in 1914” concerns the epidemiology of cardiovascular and atherosclerotic diseases. In 1982/1983, 621 men, all born in an even-number month of 1914 and residing in the city of Malmö, Sweden, were invited to the combined medical and psychological examination. Of the 500 men who participated in the study, 294 (58.5%) were hypertensive and 191 (38.2%) were normotensive. Data on blood pressure were missing for 15 (3%) men. Nonparticipation was related to lower socioeconomic background, being single, or being hospitalized. All hypertensive men with complete data in all the examinations constituted the study cohort.

The Ethical Committee of the Faculty of Medicine, Lund University, Sweden, approved the study.

Serial CWT

Background
The serial CWT is a semixperimental way to differentiate between adaptive styles in a novel and conflicting situation. Stroop designed the original CWT for studies of interference. An individual is presented a written name of a color, which is printed in a divergent color. The task is to name the color of the print and not the written word. This method of studying interference, by presenting 2 conflicting stimuli simultaneously, causes the response to become slower. The serial CWT was chosen because it is experienced as frustrating and challenging. The Stroop CWT has been used to evoke stress reactions in studies of cardiovascular reactivity.

The construction of the serial CWT was founded on a model in which perception and personality are considered a unit. Personality determines which strategies an individual uses when controlling needs, mediating between conflicting needs, or adjusting needs to reality. Through ontogenesis, certain strategies become preferred or habitual, and these characteristic strategies are also used when the individual has to adapt to new and conflicting demands. By the construction of a serial CWT, in which temporal aspects of behavior could be studied from start until final mastery, these strategies would become evident.

Administration, Scoring, and Classification
Four color words (“red,” “green,” “blue,” and “yellow”), ordered randomly in a 10 words × 10 rows design and printed on a sheet of cardboard, made up the test. The words were printed in an incongruent color. The men were asked to name the color of the print and to ignore the written word. A practice session established that the instructions were fully understood. Naming the color of the prints as quickly as possible was encouraged. The test was repeated 5 times with each repetition referred to as a “subtest.”

Scoring of each subtest was made by the test administrator after 20, 40, 60, 80, and 100 responses and was expressed as time consumption in seconds.

For the description of situational behavior, a primary classification is determined from the individual’s most frequent pattern during testing. It is based on the regression (linear change) and the variability (nonlinear change) in each subtest and on how these values relate to the medians of the group. Reference medians were obtained from the test results of the 431 men who completed the test in 1982/1983. Detailed information about the test is found in the manual, presently revised and translated into English.

In the secondary classification, on the other hand, the habitual adaptive behavior is reflected. Four patterns of adaptation are categorized according to linear change, the Regression dimension, and nonlinear change, the Variability dimension, obtained by renewed calculations of regression and variability for each subtest and compared with reference medians. The 4 patterns, which are equally labeled in both dimensions, describe adaptation as a process, from start until the end. Stabilized patterns show an even and stable time consumption through all the subtests. The cumulative patterns show increasing time consumption within subtests and from 1 subtest to the next. The dissociative patterns show a recurrently increasing and decreasing time consumption in all 5 subtests. The fourth pattern, the cumulative-dissociative, shows increasing time consumption from the first subtest until the last combined with intermittently increasing and decreasing time consumption in each subtest. More information on these adaptive patterns has been given in detail.

Blood Pressure, Hypertension, and Treatment
Blood pressure was measured in a standardized way with the individual in a sitting position. The pressure was established to the closest 5 mm Hg level with the arithmetic mean calculated from 3 consecutive measurements.

Hypertension was defined as systolic or diastolic blood pressure of ≥160/95 mm Hg or if medication for hypertension had been prescribed.

Antihypertensive treatment was recorded if drugs to lower the blood pressure had been prescribed. The use of anticoagulant medical drugs was also recorded separately.

Cerebrovascular Risk Factors
Hospital records, clinical examination by a neurologist, and answers from a questionnaire about previous diseases were used to establish history of stroke.

Peripheral artery disease was defined at an ankle-brachial blood pressure index of <0.9 in 1 or both legs.

Findings from 24-hour ambulatory ECG recordings were used to establish presence of atrial fibrillation.

Prevalent ischemic heart disease was defined as angina pectoris according to the Rose questionnaire or if the individual had been hospitalized because of myocardial infarction. Diabetes mellitus was defined as a fasting blood glucose level of ≥7.0 mmol/L or if medication for diabetes mellitus had been prescribed.

A structured questionnaire inquired about tobacco and alcohol habits. Tobacco habits were categorized as never smoked, former smokers (who had maintained current abstinence for at least the previous month), and current smokers. Similarly, alcohol habits were categorized as never uses alcohol, does not drink more than 250 g/wk, and drinks more than 250 g/wk.

Body mass index was measured as body weight in kilograms divided by height in meters squared. Plasma cholesterol level and triglyceride levels were measured according to standardized procedures and expressed in mmol/L.

Self-Reported Psychiatric Disorders
Before the examination, the men had been asked to fill in a questionnaire of medical history. One of the questions, “Has a doctor or a nurse told you that you have a psychiatric disease?” was used in this study as an indication of a psychiatric disorder. The answers were grouped according to how long the men had had a disease as never, <1 year, between 1 and 10 years, and >10 years.

Stroke and Follow-Up Data
All participants were followed from baseline examination until the first stroke occurring during follow-up, their death, or December 31, 1996. Mean follow-up time was 9.9 years (range 3.1 months to 14 years 3.4 months). A stroke incident was defined according to World Health Organization definitions. The following International Classification of Diseases, Ninth Revision (ICD-9) codes are encountered in the study: hemorrhagic stroke ICD-9 codes 430 (subarachnoid hemorrhage) and 431 (intracerebral hemorrhage) and nonhemorrhagic stroke ICD-9 codes 434 (ischemic stroke) and 436 (unspecified). The incidence of a stroke was obtained through the Stroke Registry of Malmö and hospital records. The ICD-9 codes 430, 431, and 434 were all verified by CT scanning. Data on mortality and cause of death have been continuously obtained from the Swedish National Bureau of Statistics. Stroke rates were calculated as stroke event per 1000 person-years of follow-up.
Statistical Methods
All hypertensive men with complete data from all the relevant examinations (n=243) were included in the present study. SPSS Advanced Statistics 6.1, 1994, was used for all computations. Stroke rates per 1000 person-years were calculated for the men when divided into the 4 patterns of adaptation in the serial CWT dimensions Regression and Variability. The Cox proportional hazards model was used to establish univariate relations between the serial CWT dimensions Regression and Variability and the incidence of stroke. The same procedure was used for univariate relations between each baseline variable and stroke rate. Variables with \( P \leq 0.2 \) were chosen for the final analysis. The estimation of the relative influence of adaptive pattern on stroke incidence was made in a multivariate analysis (Cox proportional hazards model) with application of the forward, stepwise procedure. Probability of entry was \(<0.05\), and probability of removal was \(>0.10\). The influence of adaptive pattern was thus analyzed in relation to peripheral artery disease, atrial fibrillation, antihypertensive drug treatment, and smoking habits. In the regression analyses, the Regression and Variability dimensions of adaptation were entered as categorical variables. The stabilized pattern of each dimension was used as a reference category. Alcohol use, smoking habits, and psychiatric disorder were likewise entered as categorical variables when part of regression analyses. Confidence intervals were calculated at the 95% level.

Results
During the follow-up, 43 (17.7%) men experienced a non-hemorrhagic stroke (ICD-9 codes 434 and 436), and 4 died within 7 days. Five (2.1%) men experienced a hemorrhagic stroke (ICD-9 codes 430 and 431), and 2 died within 7 days. Eleven (4.5%) men had a history of stroke at baseline, and 3 of them had another stroke during follow-up.

Serial CWT and Incidence of Stroke
The differential stroke rates for the men, categorized into the 4 adaptive patterns of the Regression dimension, are illustrated in the Figure. The 5 men who had hemorrhagic strokes are included in the Figure. Three of these men had an adaptive pattern in the Regression dimension categorized as dissociative, and the remaining 2 had cumulative-dissociative patterns. To confine the following analyses to the nonhemorrhagic strokes, the 5 men who had hemorrhagic strokes were excluded.

The adaptive patterns in the serial CWT dimensions Regression and Variability were analyzed in relation to incidence of stroke (Table 1). Men whose behavior in the test situation was categorized as cumulative-dissociative in the Regression dimension had a significantly increased risk of stroke during follow-up (unadjusted relative risk 2.53, 95% CI 1.13 to 5.68, \( P=0.025\)). The stroke rate for men with a cumulative-dissociative pattern in the Regression dimension was more than twice as high (31.2 strokes per 1000 person-years) than the rate of stroke for men with a stabilized pattern (12.6 strokes per 1000 person-years). No pattern in the Variability dimension was associated with stroke during follow-up.

Stroke Rate in Relation to Baseline Risk Factors
Baseline characteristics of the study cohort are given in Table 2, distributed according to adaptive pattern of the Regression dimension. Among men with a stabilized pattern, only 32.8% had been prescribed antihypertensive drug treatment. This proportion was 43.8% among those with a cumulative-dissociative pattern. The prevalence of ischemic heart disease was the lowest among men with a cumulative-dissociative pattern. Anticoagulant medical therapy (not shown in the table) had been prescribed to 2 men, and both showed stabilized patterns. When asked about psychiatric disorders, 6 men confirmed disease with a duration of 1 to 10 years, and 15 men reported a duration of \(>10\) years.

The crude relative risk of each variable in association with stroke rate is also shown in Table 2.

Multivariate Analysis
Multivariate analysis was limited to stroke incidence in relation to the 4 adaptive patterns of the Regression dimension of the serial CWT, because no univariate associations were found between the Variability dimension and stroke incidence. The multivariate analysis included the 4 patterns of
the Regression dimension, peripheral artery disease, atrial fibrillation, antihypertensive drug treatment, and smoking habits. The cumulative-dissociative pattern in the Regression dimension of the serial CWT was associated with stroke in a statistically significant way (relative risk 3.00, 95% CI 1.32 to 6.81, \( P = 0.009 \)) (Table 3). Associations were also present between stroke incidence and peripheral artery disease (relative risk 3.02, 95% CI 1.47 to 6.16, \( P = 0.003 \)) and atrial fibrillation (relative risk 2.91, 95% CI 1.02 to 8.34, \( P = 0.046 \)). Use of antihypertensive drugs or smoking habits were not associated with stroke rate.

### Discussion

Hypertensive men form a heterogeneous group regarding smoking habits, drinking behavior, blood pressure level, and the extent to which arteriosclerotic disease has developed. These factors are all related to the incidence of stroke, but heterogeneity can also be proved regarding how hypertensive men adapt in stressful situations. The conclusion of the present study is that 1 distinct pattern of adaptation, the cumulative-dissociative pattern, of the Regression dimension of the serial CWT, is associated with an increased incidence of stroke, independent of other risk factors. The specific behavior was characterized by difficulties that varied along the test situation, and for each new subtest, the linear change was accelerated. This is thought to imply that an initially tight control is exhausted by the end of the test as a result of repeated efforts and failures to find successful strategies to master the conflict.\(^{30}\)

The pathophysiological mechanisms that could explain why individual difficulties in stressful situations would be related to a future stroke are not clear, but some established relations exist between stress and disease. Although individuals vary and behavior elicited by a stressor varies, the coping mechanisms measured on the behavioral level have been associated with specific physiological correlates. Active coping behavior has been related to increased catecholamine release and sympathetic activation, whereas passive behavior has been related to corticosteroid secretion.\(^{31}\)

Cardiovascular reactivity (the manner in which the cardiovascular system responds to psychological stress) has been associated with carotid artery atherosclerosis and its progression,\(^{32}\) increased serum lipid concentrations, hemostatic factors, and blood viscosity.\(^{33}\) These factors are also related to stroke.\(^{13,34}\) An association between personality and cardiovascular reactivity has been suggested because individuals differ in reactivity when exposed to a mental stressor.\(^{3}\) It cannot be excluded that individuals whose adaptive behavior is characterized as cumulative-dissociative are more disposed to elevated blood pressure when met with stressful encounters.

McEwen and Seeman\(^{35}\) use the concepts of allostasis and allostatic load to describe both physiological and behavioral responses to stress. “Allostasis” has been defined as the ability of the organism to maintain stability through change. It is not the unique, stressful event that can be related to disease but rather the repeated and life-long exposure to stressful situations. Consequently, “allostatic load” refers to the accumulation of the wear and tear to which the different physiological systems have been exposed during a lifetime of allostasis, through either inefficient responses or having experienced many stressful events. The term is aimed at describing an individual’s total exposure to stressful events and consequences for the regulatory system. In view of this theory, it would be reasonable to assume that men with a cumulative-dissociative pattern would be exposed to greater levels of allostatic load than would men who show other adaptive patterns.

In an earlier work,\(^{21}\) based on the same study cohort of hypertensive men, the cumulative-dissociative pattern of the Variability dimension was associated with an increased risk of a cardiac event during follow-up. The aspect of control was considered important. Feelings of tension were thought to disturb the acquisition of a successful strategy to manage the stressful situation. The tension would cause intermittent breakdowns in the adaptive process and result in accumulated and enhanced nonlinear change in time consumption. In the cumulative-dissociative pattern of the Regression dimension, control is certainly of importance, but the pattern is such that
control was executed only at the beginning of the test and is running short toward the end. Despite a growing familiarity with the character of the task, attempts to find new and durable strategies are accompanied by increasing difficulties through the complete test session.

The methodological aspects that must be considered in the present study concern the medical diagnoses, foremost that of stroke, and the use of the serial CWT. At baseline, history of stroke was established by a neurologist who based the diagnosis on a questionnaire of medical history, clinical examination, and hospital records.24 Strokes that occurred during follow-up involved patients with hospital records that provided CT and autopsy results. The serial CWT has previously been used mostly in clinical settings to increase the understanding of the adaptive strategies used by individuals with various psychiatric disorders.30,36 A consistent and general observation from those studies is that control subjects more often showed a stabilized or cumulative pattern, whereas more severe psychological disturbances were associated with a higher frequency of a dissociative or cumulative-dissociative pattern in either dimension.19,36,37 In the present study, however, psychiatric disorders were not more frequent among individuals whose behavior was categorized as cumulative-dissociative.

The semiexperimental method of the serial CWT was used as a stress-inducing task in the present study, and the results were related to stroke incidence in hypertensive men during a follow-up period of 14 years. Other studies have used questionnaires to estimate experiences of stress. In a large cohort study of stroke incidence in 7000 middle-aged men, psychological stress was defined as feelings of tension and anxiety on a scale of 1 to 6. This single item was sufficient to show an independent relationship between stress and stroke during 12 years of follow-up. The present study is focused on hypertensive men but is otherwise similar in design. Both studies show that indications of perceived stress at baseline can be associated with a future stroke. Another approach to analysis of the relationship between personality traits and

<table>
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<tr>
<th>Risk Factor</th>
<th>Stabilized (n=67)</th>
<th>Cumulative (n=53)</th>
<th>Dissociative (n=54)</th>
<th>Cumulative-Dissociative (n=64)</th>
<th>Unadjusted Relative Risk*</th>
<th>95% CI</th>
<th>P</th>
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<td>History of stroke</td>
<td>3 (4.5)</td>
<td>4 (7.4)</td>
<td>3 (4.7)</td>
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<td>1.80</td>
<td>0.43−7.48</td>
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<td>13 (19.4)</td>
<td>6 (11.1)</td>
<td>11 (17.2)</td>
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<td>2.85</td>
<td>1.43−5.66</td>
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<td>Atrial fibrillation</td>
<td>3 (4.5)</td>
<td>2 (3.7)</td>
<td>2 (3.1)</td>
<td></td>
<td>3.15</td>
<td>1.12−8.85</td>
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<td>Prevalent ischemic heart disease</td>
<td>13 (19.4)</td>
<td>10 (18.5)</td>
<td>7 (10.9)</td>
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<td>0.61</td>
<td>0.22−1.72</td>
<td>0.352</td>
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<td>Antihypertensive drugs</td>
<td>22 (32.8)</td>
<td>25 (46.3)</td>
<td>28 (43.8)</td>
<td></td>
<td>1.63</td>
<td>0.90−2.98</td>
<td>0.109</td>
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<td>Diabetes mellitus</td>
<td>5 (7.5)</td>
<td>5 (9.3)</td>
<td>3 (4.7)</td>
<td></td>
<td>0.40</td>
<td>0.06−2.94</td>
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<td>8 (14.8)</td>
<td>12 (18.8)</td>
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<tr>
<td>Former</td>
<td>36 (53.7)</td>
<td>31 (48.4)</td>
<td>31 (48.4)</td>
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<td>1.03</td>
<td>0.44−2.39</td>
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<td>Current</td>
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<td>21 (32.8)</td>
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<td>2.05</td>
<td>0.89−4.71</td>
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<td>0</td>
<td>17 (25.4)</td>
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<td>≤250</td>
<td>43 (64.2)</td>
<td>43 (67.2)</td>
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<td>1.14</td>
<td>0.57−2.27</td>
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<td>&gt;250</td>
<td>7 (10.4)</td>
<td>4 (7.4)</td>
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<td>0.74</td>
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<td>Never</td>
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<td>58 (90.6)</td>
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<tr>
<td>1–10 years</td>
<td>1 (1.5)</td>
<td>1 (1.9)</td>
<td>1 (1.9)</td>
<td></td>
<td>1.34</td>
<td>0.18−0.97</td>
<td>0.774†</td>
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<td>&lt;10 years</td>
<td>5 (7.5)</td>
<td>5 (9.2)</td>
<td>4 (6.3)</td>
<td></td>
<td>1.00</td>
<td>0.31−3.23</td>
<td>0.995†</td>
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<td>Mean±SD</td>
<td></td>
<td></td>
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<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>164.3±16.4</td>
<td>165.2±18.7</td>
<td>166.2±16.2</td>
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<td>1.00</td>
<td>0.98−1.01</td>
<td>0.634</td>
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<td>Diastolic blood pressure, mm Hg</td>
<td>97.4±9.3</td>
<td>99.4±9.0</td>
<td>99.2±8.3</td>
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<td>1.01</td>
<td>0.97−1.04</td>
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<td>Body mass index, kg/m²</td>
<td>25.6±3.0</td>
<td>25.6±3.4</td>
<td>25.3±2.7</td>
<td></td>
<td>1.00</td>
<td>0.90−1.10</td>
<td>0.926</td>
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<td>Plasma cholesterol level, mmol/L</td>
<td>6.3±1.0</td>
<td>6.0±1.1</td>
<td>6.1±1.0</td>
<td></td>
<td>0.96</td>
<td>0.72−1.28</td>
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<td>Triglyceride level, mmol/L</td>
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<td>1.6±0.7</td>
<td>1.7±0.7</td>
<td></td>
<td>0.97</td>
<td>0.62−1.52</td>
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ABPI indicates ankle-brachial blood pressure.
*Cox proportional hazards model.
†Compared with the reference category of the variable.
stroke has been to compare individuals who had a stroke with healthy control subjects. Anger and the feature “high tenseness” of the type A personality have been associated with a higher prevalence of ischemic stroke. On interview of 32 men about their psychological history of stroke, Adler et al. noted that the most commonly reported factor was personal failing.

The way in which a stressful situation is managed can be associated with the incidence of stroke. It is possible to identify a subgroup of individuals who are more vulnerable than others with the serial CWT. Hypertensive men whose behavior was categorized as cumulative-dissociative in the Regression dimension were vulnerable to stress and consequently had an increased risk for stroke.

Acknowledgments
This study was supported by grants from the Swedish Council for Social Research and from research foundations administered by Malmö University Hospital. The authors are indebted to Prof Gudmund Smith (Lund University, Lund, Sweden) for valuable support in preparation of the manuscript.

References
Cardiovascular and Behavioral Reactions to Stress and Cerebrovascular Disease

Psychological stress has been implicated as both a precursor to cardiovascular disease\(^1\) and a significant risk factor for death in those with established coronary heart disease (CHD),\(^2,3\) although some counterexamples exist.\(^4,5\) There is also an extensive literature, again not all of it positive, concerning the role of behavioral factors, such as hostility and type A behavior, in the pathogenesis of CHD. In marked contrast, little attention has been paid to psychosocial factors in relation to stroke. There is preliminary evidence from one prospective study\(^7\) of a positive association between psychological stress and stroke and, from a variety of sources,\(^8\)\(^–\)\(^11\) that psychological factors may be predictive of prognosis. Such research outcomes raise the question of what psychological and behavioral mechanisms underlie links between psychological stress, on the one hand, and subsequent health outcomes, such as cerebrovascular and cardiovascular disease, on the other.

A possibility here stems from the observation of markedly and reasonably stable individual differences in the magnitude of cardiovascular reactions to a variety of mental and physical stress exposures. What has come to be called the “reactivity hypothesis” holds that exaggerated cardiovascular perturbations in response to such exposures contribute over time to the development of cardiovascular pathology. Cardiovascular reactivity has been defined as “an individual’s propensity to experience cardiovascular reactions of greater or lesser magnitude, in relation to those of other persons, when encountering behavioral stimuli experienced as engaging, challenging, or aversive.”\(^12\) The earliest and most frequently evoked version of this reactivity hypothesis implicates cardiovascular reactions to psychological stress in the etiology of essential hypertension.\(^13\)\(^–\)\(^16\) Two consistent findings from cross-sectional research support the hypothesis: (1) individuals with borderline hypertension exhibit larger-magnitude cardiovascular reactions to stress than do normotensives,\(^17\) and (2) children of hypertensive parents appear to experience greater elevations in blood pressure in response to stress.\(^18,19\)

However, there is some uncertainty about the exact nature of the risk conferred by excessive cardiovascular reactivity,\(^2,15,20\) as well as doubts expressed regarding the stability of individual differences in cardiovascular reactivity across time and different eliciting stimuli, as well as the generalizability of reactions to laboratory challenges to reactions to everyday life stress exposures.\(^15,20\) Nevertheless, empirical evidence attests that laboratory measures of cardiovascular reactivity exhibit acceptable temporal and intertask consistency and generalize reasonably well to real life reactivity.\(^21\)\(^–\)\(^23\)

Several prospective studies have now examined the relationship between cardiovascular reactivity to a range of laboratory challenges and subsequent cardiovascular disease. Three main types of laboratory stress have been deployed: (1) the cold pressor test,\(^24,25\) (2) mental stress (for example, Raven’s matrices, Color-Word Test, mirror-image tracing),\(^26,27\) and (3) the anticipation of exercise.\(^28\)\(^–\)\(^30\) In addition, a variety of disease outcomes have now also been examined, including carotid atherosclerosis,\(^31\)\(^–\)\(^33\) left ventricular mass,\(^34,35\) cardiovascular disease,\(^25,36\) and more recently, stroke.\(^30\) However, given the original focus of the reactivity hypothesis it is perhaps hardly surprising that the bulk of studies targeted blood pressure and hypertension as outcomes.\(^24,26,28,37\)

Two recent prospective studies in Stroke have examined cardiovascular reactions to stress in healthy men\(^30\) and behavioral adaptations to stress in hypertensive individuals in relation to incident stroke (discussed in the article preceding this editorial comment). Everson et al.\(^30\) examined the association between blood pressure reactivity to the anticipation of bicycle exercise and subsequent incident stroke in 2303 men from the Kuopio Ischaemic Heart Disease Risk Factor Study in Finland. Men with elevated systolic blood pressure reactivity (≥20 mm Hg) had a 72% greater risk of any stroke and an 87% greater risk of ischemic stroke relative to less reactive men.

The more recent of these 2 studies, the preceding article by Andrén-Pettersson et al., explored in 238 hypertensive men born in 1914 in Malmö, Sweden, patterns of behavioral adaptation to a psychological stressor (Color-Word Test), a cognitive conflict task, and the subsequent incidence of stroke. Men who exhibited what the authors called a cumulative-dissociative pattern of behavior in response to the test had a more than 2-fold increased risk of suffering a stroke during follow-up. A cumulative-dissociative behavior pattern is described as “an initially tight control that, as a result of repeated efforts and failures to find successful strategies to master the conflict, is exhausted by the end of the test.” An earlier study of the same cohort\(^38\) found that this cumulative-dissociative adaptation to stress was also associated with increased risk of cardiac events. Thus, healthy men with elevated cardiovascular reactions to stress and hypertensive men who adapt poorly to stressful situations may be more vulnerable to stroke.

The association between the magnitude of cardiovascular reactions to stress and behavioral adaptations to stress in this context remains to be determined. Furthermore, because the findings of these 2 studies have important theoretical and clinical implications, replication is important. The somewhat variable results that have emerged from the study of cardiovascular reactivity and other outcomes further reinforce the need to establish the robustness of the results for stroke.
The earliest studies of cardiovascular reactivity and hypertension employed the cold pressor test, a passive stress task. The pattern of results is best described as mixed; there are as many studies that have not found a relationship, including some on large cohorts, as studies that have.29 Prospective studies that have used active mental stress tasks provide somewhat more consistent evidence for the reactivity hypothesis. However, the effects tend to be variable, and in some cases of doubtful clinical prognostic significance; approximately 1% to 6% of the variance in follow-up blood pressure or blood pressure change is accounted for by blood pressure reactions to an active mental stress task, following adjustment for basal blood pressure at entry and other potential confounders.30,31,32 Effects of a similar order emerged from the Kuopio Study, in which blood pressure reactions were measured in response to anticipation of physical exercise. It is worth noting here that exercise anticipation is unlikely to be analogous to the usual laboratory mental stress tasks in terms of both psychological and physiological demands.40 Furthermore, the magnitude of such anticipatory cardiovascular reactions are related to physical training history, which will be reflected in variations in physical fitness. The association between fitness levels and cardiovascular pathology is very well documented. There are far fewer population studies of cardiovascular reactivity and subsequent cardiac events or cardiac mortality. The results are again mixed, with more studies failing to find a relationship than reporting one.25 The indications from studies of carotid atherosclerosis31-33 and left ventricular mass34,35 are promising, but the data are few and it is not at all clear that the latter outcome is related to the former and that it has significance for disease end points.

The findings from the 2 recent prospective studies published in Stroke which suggest, first, that the magnitude of cardiovascular reactions to a challenging exposure is associated with incident stroke in initially healthy men (Everson et al36), and second, that stroke incidence is related to the manner in which hypertensive patients behaviorally adapt in the face of a stressful mental challenge (Andre-Pettersson et al), are exceedingly encouraging. The brief review above of cardiovascular reactivity studies using other disease outcomes, however, suggests caution. The history of studies implicating other behavioral adaptations to stress, such as type A behavior, in cardiovascular disease should act as a further warning that encouraging early indications in this field do not always stand the test of time and replication. Nevertheless, we hope that other researchers will react adaptively to the challenge of these data. Although substantially neglected, the issue of whether the patterns of cardiovascular and behavioral adjustments to psychological stress are implicated in stroke is far from trivial.

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Adaptive Behavior in Stressful Situations and Stroke Incidence in Hypertensive Men: Results From Prospective Cohort Study "Men Born in 1914" in Malmö, Sweden

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Stroke. 2001;32:1712-1720
doi: 10.1161/01.STR.32.8.1712

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/32/8/1712

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